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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY. DOCKET NO.	CONFIRMATION NO.
10/821,333	04/09/2004	Bret A. Shirley	PP17201.018 (035784/27729	9990

27476 7590 04/02/2007

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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	**PAPER NUMBER**
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,333	SHIRLEY ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/12/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is response to Applicant's reply filed 1/2/07 to the requirement for species election without traverse. Applicant elects "aspartic acid" as the species of buffer to prosecute. Claims 1-24 are pending and examined.

Priority

2. Applicant is required to update the priority information by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Specification

3. The use of the trademark Millipore, Labscale and Biomax has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see for example, p. 17). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

5. There is a blank space on page 21, line 22.

Information Disclosure Statement

6. The IDS submitted 7/12/2004 has been considered.

Claim Rejections - 35 USC § 112

7.The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7a. Claims 1, 9, 15 and 20 are rejected because the claims encompass "biologically active" variants. The specification states on p. 18, lines 20-21 that biologically active variants of IFN-β encompassed by the invention should retain IFN-β activities, particularly the ability to bind to IFN-β receptors. This statement does not serve to define such variants because it only lists preferred, not required properties. Thus the artisan would be unable to determine what properties, and thus what molecules, Applicant intended the claims to encompass. Claims 2-8, 10-14, 16-19 and 21-24 are rejected insofar as they are dependent on rejected claims 1, 9, 15 and 20.

Claim Rejections - 35 USC § 103

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8a. Claims 1-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hershenson et al. (5, 004, 605, PTO1449 of 7/12/2004) in view of Merck Index, 1983, p.121, column 2.

The instant invention is drawn to stabilized HSA-free pharmaceutical composition comprising substantially monomeric IFN-β or biologically active variants. The

formulation of this composition is to contain an ionic strength that is not greater than 60mM and it further contains trehalose.

Hershenson et al. teaches stable compositions of IFN-β, including recombinant IFN-β and the mutant IFN-β_{ser17} (columns 1 and 2). Both glycosylated and bacterially produced or non-glycosylated forms are taught (columns 1 and 2, column 7, lines 2-3). Hershenson et al. teaches compositions of these forms at pH 2-4, at a buffer concentration of 1-50 mM, which is less than the ionic strength of 60mM (column 4, lines 39-59). Interferon concentrations of .05- 10 mg/ml are taught (column 8, lines 61-65). Hershenson et al. teaches the use of polyethylene glycol as a stabilizing agent but also teaches that trehalose can be used as a stabilizer at concentrations of .025-10% (column 9, lines 21-31). Although, the reference teaches the use of phosphoric acid, glycine and citric acid as buffers (column 21) Hershenson et al. fails to teach the use of aspartic acid as a buffer. The Merck Index teaches that aspartic acid has a pK_2 of 3.65.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art to use aspartic acid disclosed in the Merck Index to buffer the formulations taught by Hershenson et al. One of ordinary skill would have been motivated to use aspartic acid for buffering because it has optimal buffering capacity at the pH range taught by Hershenson et al. Further, there is reasonable expectation of success because Hershenson et al. disclose acids similar aspartic acid in the formulations. Therefore, the instant invention is *prima facie* obvious over Hershenson et al. (5, 004, 605) in view of Merck Index, 1983, p.121, column 2.

8b. Claims 1-24 are rejected under 35 U.S.C. 103(a) as being obvious over Hershenson et al. (5, 004, 605) in view of Chen et al. (6, 525, 102, PTO1449 of 7/12/2004).

The applied reference has a common inventor and assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The instant invention is drawn to stabilized HSA-free pharmaceutical composition comprising substantially monomeric IFN-β or biologically active variants. The formulation of this composition is to contain an ionic strength that is not greater than 60mM and it further contains trehalose.

Hershenson et al. teaches as set forth above in paragraph 8a but fails to teach the use of aspartic acid. Chen et al. teaches stabilized compositions of IFN-β, including IFN-β_{ser17} in column 12, lines 29-32, arid column 19, lines 30-40. That aspartic acid can be used in stabilizing these compositions is taught in column 5, lines 4, 20-56. Thus, it would have been obvious to one of ordinary skill in the art to combine the teachings of Hershenson et al. and Chen et al. to use aspartic acid as a buffer in the compositions of Hershenson et al. One of ordinary skill would be motivated to do so because Hershenson et al. teaches stabilized compositions of IFN-β and Chen et al. teaches a buffer useful for IFN-β that also has stabilizing properties. Thus one of ordinary skill would have expected the buffer taught by Chen et al. to work at least as well as those exemplified by Hershenson et al. Therefore, the instant invention is *prima facie* obvious over Hershenson et al. (5, 004, 605) in view of Chen et al. (6, 525, 102).

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9a. Claims 1-24 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 8, 10, 11, 15, 16, 31-40, 61-64, 68-71, 74, 75-78, 92-94 and 96 of U.S. Patent No. 6, 887, 462. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to stabilized HSA-free pharmaceutical composition comprising substantially monomeric IFN-β or biologically active variants containing an ionic strength that is not greater than 60mM and further containing trehalose which are encompassed by the allowed claims of '462 patent. Specifically, an ionic strength that is not greater than 60mM as disclosed in the instant invention will also include the ionic strength that is not greater than 20mM that is disclosed in the in the allowed patent. Further, the allowed patent composition also comprises trehalose that is disclosed in the instant invention. In addition, as in the instant claims aspartic acid is used for buffering in the allowed patent. Therefore, claims 1-24 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 8, 10, 11, 15, 16, 31-40, 61-64, 68-71, 74, 75-78, 92-94 and 96 of U.S. Patent No. 6, 887, 462.

9b. Claims 1-24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5, 7- 20 and 22 of copending Application No. 11/062, 146 ('146). Although the conflicting claims are not identical, they are not patentably distinct from each other because an ionic strength

that is not greater than 60mM as disclosed in the instant invention will also include the ionic strength that is not greater than 20mM that is disclosed in the in the '146 application. In addition, aspartic acid also used as buffer in both claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. No claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JS
Art Unit 1647
March 29, 2007.

Patent Examiner